The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: 114454 (FLU D-PAN H1N1-AS03-043)

Title: Immunogenicity and safety of Fluarix™/ Influsplit SSW® 2010/2011 or Pandemrix™.
Fluarix™/ Influsplit SSW® 2010/2011 (Flu): GlaxoSmithKline (GSK) Biologicals' trivalent inactivated seasonal influenza split vaccine.
Pandemrix™ (H1N1): GSK Biologicals' adjuvanted pandemic influenza vaccine.

Rationale: The aim of this study was to assess the immunogenicity and safety following administration of Flu or H1N1 vaccine in adults previously vaccinated with 1 dose of H1N1 vaccine.
The study was prematurely terminated not because of safety issues or lack of immunogenicity but for logistic reasons.

Phase: III

Study Period: 27 August 2010 to 28 February 2011.

Study Design: Open, randomised, multi-centric, single-country study with 3 parallel groups.

Centres: 2 centres in Germany.

Indication: Immunisation against influenza in male and female adults aged 18 years and above.

Treatment: The treatment groups were as follows:

- PAN Group: Subjects who were previously vaccinated with H1N1 vaccine received 1 dose of H1N1 vaccine.
- Flu Group: Subjects who were previously vaccinated with H1N1 vaccine received 1 dose of Flu vaccine.
- CTRL Group*: Subjects who were not previously vaccinated with H1N1 vaccine received 1 dose of Flu vaccine.

All vaccines were administered intramuscularly in the deltoid region of the non-dominant arm on Day 0.
*The study was prematurely terminated; only 7 subjects were enrolled in either PAN Group or Flu Group. No subject was enrolled in the CTRL Group

Objectives:

- To evaluate the humoral response in terms of haemagglutination inhibition (HI) antibodies against each influenza vaccine strain corresponding to the influenza vaccine administered, at Day 21, in subjects aged 18-60 and above 60 years.

Primary Outcome/Efficacy Variable:

- Humoral immune response in terms of HI antibodies for each vaccine strain, 21 days after vaccination in subjects aged 18-60 and above 60 years.

Derived variables:

- Geometric Mean Titre (GMT) and seropositivity rates at Day 21
- Seroconversion Rate (SCR*) at Day 21
- Seroprotection Rate (SPR**) at Day 21
- Mean Geometric Increase (MGI***) at Day 21

SCR*: is defined as the proportion of subjects who have either a pre-vaccination reciprocal HI titre < 1:10 and a post-vaccination reciprocal titre ≥ 1:40, or a pre-vaccination reciprocal HI titre ≥ 1:10 and at least a 4-fold increase in post-vaccination reciprocal titre against the vaccine virus.
SPR**: is defined as the proportion of subjects with reciprocal HI titres ≥ 1:40 against the vaccine-homologous virus. The Committee for Human Medicinal Products (CHMP) criterion is fulfilled if the post-vaccination point estimate for SPR is > 70% in subjects 18 to 60 years of age or > 60% for subjects > 60 years of age.
MGI*** is defined as geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre. The criterion is fulfilled if the point estimate for MGI is > 2.5 in subjects 18 to 60 years of age or > 2 for subjects > 60 years of age.

Note: Data related to the primary outcome were not analysed

Secondary Outcome/Efficacy Variable(s):
*Immunogenicity**

- Humoral immune response in terms of HI antibodies against each vaccine strain, at different time points in subjects aged 18-60 and above 60 years.
  Derived variables:
  - GMTs and seropositivity rates at Days 0, 7 and 182.
  - SCR at Days 7 and 182.
  - SPR at Days 0, 7 and 182.

- MGI at Days 7 and 182.

Safety

- Solicited local and general symptoms*
  - Percentage, intensity and relationship to vaccination of solicited local and general symptoms (any and grade 3) within 7 days (Day 0 – Day 6) after vaccination.
- Unsolicited adverse events (AEs)
  - Percentage, intensity* and relationship to vaccination* of unsolicited AEs within 31 days¥ (Day 0 - Day 30) after vaccination.
- Serious adverse events (SAEs)
  - Occurrence of SAEs during the whole study period.
- potential Immune Mediated Diseases (pIMDs)*
  - Occurrence of pIMDs during the whole study period.

AEs of specific interest for safety monitoring, also called potential immune-mediated diseases (pIMDs), are a subset of AEs that include both clearly autoimmune diseases and also other inflammatory and/or neurologic disorders which may or may not have an auto-immune aetiology.

¥ Unsolicited AEs were tabulated within 30 days.

* Data were not analysed

Statistical Methods:

Since only 7 subjects were recruited in the study, the statistical analysis was not performed as defined in the protocol; only individual data listings for these 7 subjects have been generated.

Results about safety (unsolicited adverse events and serious adverse events) presented below on the Total Vaccinated cohort were based on the individual data listings).

The Total Vaccinated cohort included all subjects with vaccine administration documented.

The safety data were summarised on the Total Vaccinated cohort.

The percentage of subjects reporting AEs within 30 days following vaccination was summarised per group. The percentage of SAEs was summarised per group during the whole study period.

Study Population: Healthy male or female subjects 18 years and above, who had not received previous administration of any influenza vaccine within 6 months prior to vaccination and had received one dose of H1N1 vaccine at least 6 months before enrolment, were enrolled in the PAN or Flu groups. Female subjects of childbearing potential had to practice adequate contraception for 30 days prior to vaccination and continue adequate contraception from study inclusion up to 2 months after vaccination and had to have a negative pregnancy test on the day of vaccination. Written informed consent was obtained from the subject before study entry.

Number of Subjects:	**PAN Group**		**Flu Group**	
	18 to 60Y	**>60Y**	**18 to 60Y**	**>60Y**
Planned, N	120		120	
Randomised, N (Total Vaccinated cohort)	1	3	1	2
Completed, n (%)	1 (100)	3 (100)	1 (100)	2 (100)
Total Number Subjects Withdrawn, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawn due to Adverse Events n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawn due to Lack of Efficacy n (%)	Not applicable	Not applicable	Not applicable	Not applicable
Withdrawn for other reasons n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Demographics	**PAN Group**		**Flu Group**	
	18 to 60Y	**>60Y**	**18 to 60Y**	**>60Y**
N (Total Vaccinated cohort)	1	3	1	2
Females: Males	1:0	2:1	0:1	2:0
Mean Age, years (SD)	46 (-)	NA	30 (-)	NA
White-Caucasian / European Heritage, n (%)	1 (100)	3 (100)	1 (100)	2 (100)

- = No SD could be computed given the too small number of subjects per group
NA= Data not available in the individual listings

Primary Efficacy Results: Data were not analysed		
Secondary Outcome Variable(s): Data were not analysed		
Safety results: Number (%) of subjects with unsolicited adverse events within 30 days (Day 0 - Day 29) after vaccination. (Total Vaccinated cohort)		
Most frequent adverse events - On-Therapy (occurring within Day 0-29 following vaccination)	**PAN Group N=4**	**Flu Group N=3**
Subjects with any AE(s), n (%)	0 (0.0)	2 (66.7)
Safety results: Number (%) of subjects with serious adverse events during the whole study period (Total Vaccinated cohort)		
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]		
All SAEs	**PAN Group N=4**	**Flu Group N=3**
Subjects with any SAE(s), n (%) [n assessed by investigator as related]	1 (25.0) [0]	0 (0.0) [0]
Fatal SAEs	**PAN Group N=4**	**Flu Group N=3**
Subjects with fatal SAE(s), n (%) [n assessed by investigator as related]	0 (0.0) [0]	0 (0.0) [0]

Conclusion:
No statistical analyses were performed in this study as only 7 subjects were enrolled. Within 30 days after vaccination, 2 subjects in the Flu Group reported at least one unsolicited AE. One subject in the PAN Group reported 1 non fatal SAE during the study; the SAE was assessed by the investigator as not related to the study vaccination.

Date updated: 03-September-2014